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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,428	05/10/2005	Jeffrey Keller Teumer	50393/004001	5032

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EXAMINER	
DAVIS, RUTH A	
ART UNIT	**PAPER NUMBER**
1651	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,428	TEUMER ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-21 and 29-50* is/are pending in the application.

4a) Of the above claim(s) *34-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-21,29-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response filed on January 25, 2007 have been received and entered into the case. Claims 2 – 6 are canceled; claims 1, 7 – 21 and 29 – 50 are pending; claims 34 – 50 are withdrawn from consideration; claims 1, 7 – 21 and 29 – 33 have been considered on the merits. All arguments have been fully considered.

Claim Rejections - 35 USC § 112

Rejections under 35 U.S.C. 112, second paragraph, are withdrawn due to amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 7 – 21 and 29 – 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/01034 and WO 00/69449 in view of Keller et al (Frontiers in Bioscience, 1996), Hibberts et al (Journal of Endocrinolgy, 1998) and Van Nispen (US 5,002,881, 1991).

Applicant claims a method for cultivating hair inductive cells. The method comprises the steps of culturing the hair inductive cells, dermal papilla cells, in a non-epidermal tissue (non-ectodermal) of mesodermal or endodermal origin derived cell conditioned culture medium in which the hair inductive potential of the hair inductive cells is maintained. The conditioned cells are prostate epithelial cells or human dermal fibroblasts or may also be obtained using a cell line, which is derived from a donor who has been screened and tested for risk factors associated with transplantation.The hair inductive cells are allogeneic or autologous to the non-epidermal tissue. The medium is to consist essentially of the conditioned medium, is free of recombinant genes or products thereof, viral vectors and is concentrated by ultrafiltraion. The medium is preferably frozen prior to use. The method further comprises the step of harvesting or isolating cultured or subcultured hair inductive cells.

WO 99/01034 discloses a method for producing new hair growth comprising culturing human dermal papilla cells in a medium conditioned with human keratinocytes. They show that co-cultivation allows rat papilla cells to retain their hair inducing capabilities through 56 passages (p.2, lines 7-10). WO'034 disclose that the human papilla cells cultured in a

keratinocyte conditioned medium can expand rapidly for many passages in vitro while maintaining their hair inducing properties (p.2,lines 27-29). The keratinocytes are preferably taken from the outer root sheath of the hair follicle where the epithelial stem cells are thought to reside, i.e non-epidermal. The keratinocytes may be autologous or allogenic in source (p.4, lines 10-22). After culturing the papilla cells in the keratinocyte conditioned media, the papilla cells are then harvested and can be used directly or centrifuged, i.e. concentrated (p.5, lines 1-4).

Although, WO'034 does not specifically teach the number of passages of the dermal papilla cells, they do teach that the cells can expand for many passages and further teach the ability of rat cells under the same conditions to retain their hair inducing properties through 56 passages. Thus, it would be obvious to one of ordinary skill in the art at the time the invention was made to cultivate dermal papilla cells in a conditioned medium with cells of non-epidermal origin and expect success in maintaining the hair inducing properties through passages of more than seven.

WO 00/69449 disclose conditioned cell culture medium compositions and their methods of use. The medium may be conditioned with **any eukaryotic cell type** (p.5,lines 30-34) including human hair papilla cells (p.45,lines 34),epithelial cells, stromal, parenchymal, mesenchymal cells, liver reserve cells, neural stem cells, pancreatic stem cells, fibroblasts including human dermal fibroblasts, endothelial cells, pericytes, macrophages, monocytes, plasma cells, mast cells, adipocytes, chondrocytes, keratinocytes (p.5,lines 32-35,p.8,lines 8-12,p.9 lines 31-35) from corresponding tissues including bone marrow, skin, liver, pancreas, kidney as well as **genitourinary tract**, i.e. encompassing the prostate (p.12,lines 13-20). Cell lines may also be used in the conditioned medium but are carefully screened for human and

animal pathogens, i.e tested for risk factors associated with transplantation (see p.14,lines 6-10). The medium may contain, but does not require the addition of additional growth factors and proteins, i.e, consisting essentially of the conditioned medium (p.13, lines 8-12) and is serum-free (p.11, lines 4-7). The medium may be in any form such as liquid, frozen, lypholized, or dried (p.6,lines 18-20). The compositions are used to culture cells and further is formulated for methods of stimulating hair growth (p.7, lines 18-31). The conditioned medium is also concentrated by any methods known in the art (p.29,lines 1-9, p.46 lines 2-3).

Neither reference teaches cultivating hair inductive cells such as dermal papilla or sheath cells in conditioned medium conditioned with prostate epithelial cells. However, WO 00/69449 strongly suggests a culture media used for cultivation of cells used in a method for stimulating hair growth, particularly they disclose a media conditioned with cells from the genitourinary tract, i.e. prostate epithelial cells, which is formulated to culture cells used in methods of stimulating hair growth. Given what is known in the art of the importance of dermal papilla cells in the development of hair, it would be obvious to one of ordinary skill in the art at the time of the invention to cultivate dermal papilla cells in a conditioned medium formulated for stimulating hair growth. Further, It is known in the art that the development of the hair follicle depends on a mesenchymal-epithelial interaction, i.e dermal papilla-keratinocytes. The same is true for prostate tissue, i.e. prostate stroma-prostate epithelial cells, as is disclosed by Keller et al (Frontiers in Bioscience, 1996). It is also known that androgen plays a role in the development of both. For example, activated andogen receptors suppress the growth of follicle populations in those exhibiting male pattern baldness and altered androgen receptors have been linked to recurrence of prostate cancer (Keller, p.2). Further, as is known in the art, the development of

hair follicles is intimately associated with dermal papilla cells as is androgen through androgen receptors, which are known to effect hair follicle proliferation by modulating dermal papilla activity through growth factors. Androgen also modulates expression of growth factors in the prostate stroma (mesoderm) (p.7).

Hibberts et al (Journal of Endocrinolgy, 1998) disclose that androgens are the most obvious regulators of normal hair growth and are a prerequisite for male pattern baldness. As is known in the art, the hair follicle is composed mainly of epithelial cells which protrudes down to the epidermis and dermis of the skin, enveloping at the base the mesenchyme-derived dermal papilla cells. Androgens act on the hair follicle via the mesencyme-derived dermal papilla, altering the production of mitogenic factors and extracellular matrix factors, which influence the epithelial cells. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have cultivated hair inductive cells such as dermal papilla cells in a medium conditioned with prostate epithelial cells because it is known in the art that both hair follicles and the prostate develop via mesenchymal-epithelial interactions, i.e dermal papilla-keratinocytes and prostate stroma-prostate epithelial cells and both hair follicle and prostate development are androgen modulated, plus there has been an observed association between men with male pattern baldness and benign prostate hyperplasia (see Oh et al, Urology, vol 51 1998), therefore, one would expect to establish the required mesenchymal-epithelial interaction between dermal papilla cells and prostate epithelial cells required for hair follicle development. One of ordinary skill in the art would have been motivated to condition a hair inductive cell medium with prostate epithelial cells to achieve a mesenchymal-epithelial interaction necessary for the development of hair follicles given that both prostate and hair cell development depend on this

interaction and are androgen mediated. Thus, one would have expected success in cultivating hair inductive cells in the presence of this specific epithelial cell.

Neither reference teach concentrating the medium by ultrafiltration, however, ultrafiltration is known in the art as a concentration method used in concentrating mediums, as evidenced by US 5,002,881, which teaches using ultrafiltration to concentrate a medium (see col.3 lines 30-40).

Response to Arguments

Applicant argues that the references do not teach the method using prostate epithelial cells; that there is no motivation to combine the instant references; that the examiner uses improper hindsight and argues the references individually.

However, these arguments fail to persuade for the following reasons.

Regarding the use of prostate epithelial cells, WO 00/69449 clearly teaches mediums conditioned with **any eukaryotic cell type** (p.5,lines 30-34). The reference further suggests human epithelial cells and cells that may be obtained from **genitourinary tract**, i.e. encompassing the prostate (p.12,lines 13-20). The combination of references clearly suggest that the instant cells can be used in conditioning media, which in turn can be used to culture hair inductive cells.

Regarding applicant's argument to lack of motivation, the combination of reference cited in the rejection above demonstrates that the claimed methods were known in the art. Specifically in that culturing hair inductive cells in conditioned media was known in the art. Further, it

would have been obvious to use the prostate epithelial cells, as the references demonstrate such cells could be used. Regarding the supporting references, these references are relied upon to demonstrate that the particulars of the method were known and routinely practiced in the art at the time the claimed invention was made.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Finally, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tiffany M. Gough whose telephone number is 571-272-0697. The examiner can normally be reached on M-F 7:00 - 2:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

RUTH DAVIS
PRIMARY EXAMINER

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

tmg

RUTH DAVIS
PRIMARY EXAMINER